

The effect of template selection on diffusion tensor imaging voxel based analysis results

W. Van Hecke^{1,2}, C. Sage², J. Sijbers³, S. Sunaert², and P. M. Parizel¹

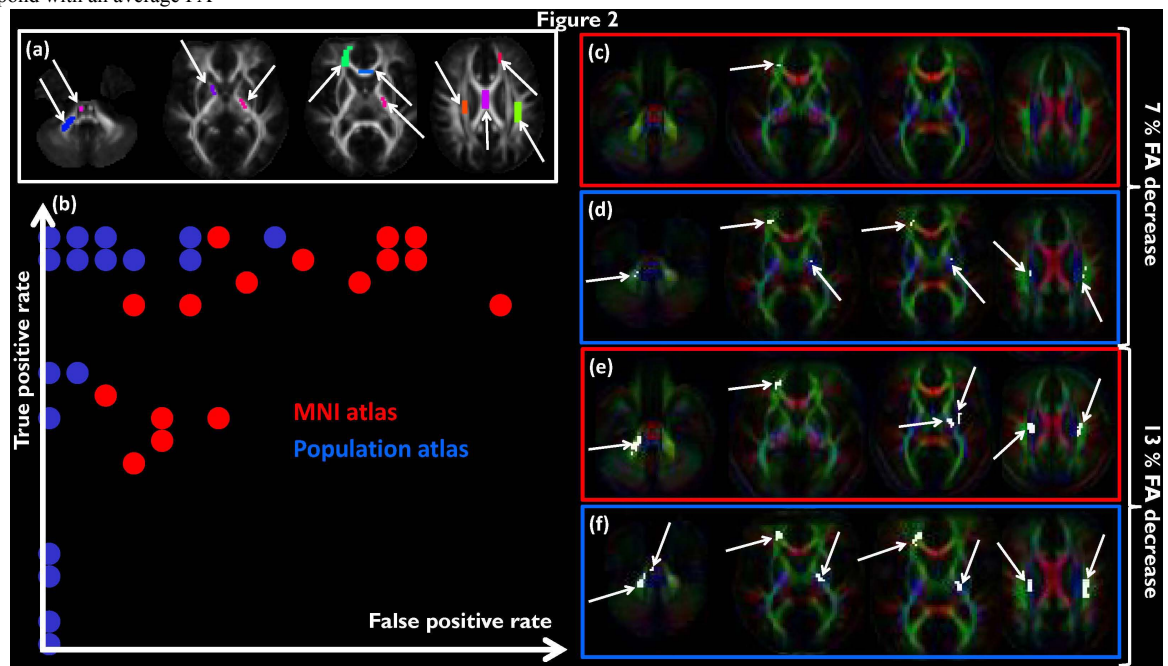
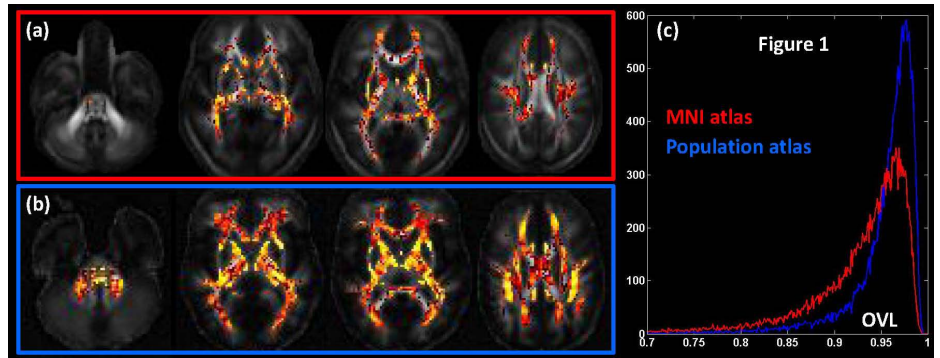
¹Department of Radiology, Antwerp University Hospital, Antwerp, Belgium, ²Department of Radiology, Leuven University Hospital, Leuven, Belgium, ³VisionLab, University of Antwerp, Antwerp, Belgium

Introduction: In recent years, voxel based analysis (VBA) studies have demonstrated the potential of diffusion tensor imaging (DTI) to detect white matter (WM) damage in patients with various neurological or psychiatric disorders. In VBA, all DTI data sets are transformed to an atlas or template, whereafter the diffusion measures of control subjects and patients are evaluated in each voxel. In most VBA studies of DTI data sets, a standard template, such as the Montreal Neurologic Institute (MNI) atlas, is used. The advantage of the MNI atlas is that it contains coordinate, anatomic, and cytoarchitectonic labels and that the VBA results can be easily compared across studies using the MNI coordinates. However, since this atlas is not study-specific, it might fail to provide a good representation of the population that is studied, thereby potentially resulting in residual image misalignment after coregistration of the DTI data sets to this reference space. Furthermore, since the original MNI template only contains anatomical MR or FA information, many studies only use the T₁, T₂, or FA as input information for the coregistration algorithm. This can affect the reliability of the VBA results, since it has been demonstrated that the use of tensor information during coregistration significantly improves the DT image alignment [1,2]. Recently a population based, study specific DTI atlas was introduced, whereby the magnitudes of the deformation fields that are needed to warp the different images to the atlas are minimized, potentially leading to a decreased image misalignment in VBA [3]. The goal of this work was to

examine the effect of the atlas selection on the reported VBA results. To this end, the VBA sensitivity and specificity to detect WM damage is investigated using simulated DTI data sets [4]. The effect of two atlases on the VBA results is examined: a DTI atlas in MNI space and a population based, study specific DTI atlas, both including all DT information in the atlas space.

Methods: 20 healthy subject and 20 patient simulated DTI data sets were constructed using the method of Van Hecke et al. [4], which was already applied in [5]. In this study, the transverse diffusivity, i.e. the average of the second and third eigenvalues, was increased by seven different levels to simulate a microstructural breakdown in 19 WM structures of the 20 patient data sets. These seven levels of pathology correspond with an average FA decrease of 4%, 7%, 10%, 13%, 16%, 19%, and 22%.

In each experiment, 160 DTI data sets were constructed: 20 healthy subject data sets and 20 patient data sets with 7 different levels of pathology. This experiment was repeated 5 times, whereby the estimation of the inter-subject variability and the noise distribution were varied. All these simulated data sets were aligned to both atlases using an affine and a non-affine registration method, based on a viscous fluid model that includes all tensor information. After the image registration to the atlases, the data sets were smoothed with an anisotropic kernel with a FWHM of 3 mm. FA values were then compared between the healthy and the simulated DTI data sets in atlas space using a non-parametric Mann-Whitney U test and a multiple comparisons correction based on the Benjamini-Hochberg false discovery rate of 0.05 was applied.



Results: In Fig. 1, the mean overlap of eigenvalue-eigenvector pairs (OVL) between all registered data sets and the MNI and population atlas is shown in (a) and (b), respectively. As is also demonstrated in Fig. 1(c), the OVL is significantly higher after registration to the population space. As a result, the sensitivity and specificity to detect the ground truth FA changes is higher after image alignment to the population atlas compared to the MNI atlas. In Fig. 2(a), the size, shape, and location of the simulated FA changes are depicted on 4 axial FA slices. The true and false positive rate of detecting the pathologies after coregistration to MNI and population space are depicted in Fig. 2(b) in red and blue, respectively. The VBA results after image alignment to MNI space and population space are shown on the same 4 axial, color-encoded FA slices in Fig. 2(c) and (d) for an FA decrease of 7% and in Fig. (e) and (f) for an FA decrease of 13%, respectively. The FA changes that were detected on the 4 axial slices are indicated by the white arrows.

Discussion: Our results suggest that the selection of the DTI template for a VBA group analysis affects the sensitivity and specificity to detect FA changes. A higher true positive rate and lower false positive rate was observed using the population atlas. This can be explained by the fact that this atlas is a better representation of the subject group that is studied, which in turn leads to smaller image registration errors.

References: [1] Park et al., 2003 (NeuroImage); [2] Van Hecke et al., 2007 (IEEE TMI); [3] Van Hecke et al., 2008 (NeuroImage); [4] Van Hecke et al., 2009a (NeuroImage); [5] Van Hecke et al., 2009b (Hum Brain Mapp)